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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,432	04/13/2004	Scott Phillip Baron	PC18327A	5027

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WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/823,432	BARON ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *2-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09.27.2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction of invention

Applicant's election without traverse the invention Group I comprised of claim 1 drawn to a genetically modified, non-human mammal comprising α2/δ1 gene comprising 290-like mutation for further prosecution on merits in the reply filed on 10/05/2006 is acknowledged.

Claims 2-40 are withdrawn from consideration

Claim 1 is pending and presently under examination.

Specification

Priority: If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim

filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Abstract: Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract filed April 13, 2004 only has 20 words. It is noted that the abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. Appropriate correction is required.

The abstract recitation of the phrase "an α2/δ2 and /or an α2/δ2 gene" makes it indefinite. Appropriate correction is required. Changing the above phrase to "one or both the alleles of α2/δ2 gene" is suggested.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a asserted utility or a well established utility.

The claim is drawn to genetically modified, non-human mammals comprising α2/δ1 gene comprising 290-like mutation.

The specification fails to disclose any phenotype of the claimed non-human mammal. A non-human mammal having no phenotype is indistinguishable from a wild-type non-human mammal and does not have a specific and substantial utility or a well-established utility because one skilled in the art would not know where and what to look for in using said non-human mammal. Absent the phenotype of the claimed non-human mammal and the correlation between a phenotype of the claimed non-human mammal and a particular disease or disorder, no "real world" use of the claimed non-human mammal has been established. Therefore, the claimed non-human mammal lacks a specific and substantial or a well-established utility. In light of the above, the skilled artisan would not find the utility of the non-human mammal encompassed by the claims to be specific and substantial or well established. And one skilled in the art clearly would not know how to make and use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the recitation of phrase "290-like mutation" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "290- like mutation") with reference to or as applicable to α2/δ1 gene, thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to genetically modified, non-human mammals comprising α2/δ1 gene comprising 290-like mutation.

The scope of invention as claimed encompasses any and/or all transgenic non-human mammals, such as mice, rats, rabbits, sheep, pigs, canine, feline, monkeys, kangaroos, echidnas, whales, other mammals etc., expressing a alpha2/delta1 transgene with a 290-like mutation. The claims encompass numerous transgenic non-human mammals having unknown and/or unidentified phenotypes or having no phenotype.

The specification fails to disclose any phenotype of the claimed non-human mammals comprising α2/δ1 gene comprising 290-like mutation. The specification only teaches a transgenic mouse comprising α2/δ1 gene comprising a 217 mutation.

The phenotypes of the various claimed transgenic non-human mammals were unpredictable at the time of the invention. The structural features and phenotypes of the transgenic non-human mammals comprising α2/δ1 gene with a 290-like mutation that can distinguish from corresponding wild-type mammal have not been disclosed. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attributes or characteristics that identify the claimed transgenic and chimeric non-human mammals, and because the claimed transgenic and chimeric non-human mammals are highly variant, the disclosure in the present application is insufficient to describe the claimed transgenic non-human mammals comprising α2/δ1 with 290-like mutation.

This limited information is not sufficient to reasonably convey to one skilled in the art that applicants were in possession of the claimed transgenic and chimeric non-human mammals. Thus, it is concluded that the written description requirement is not satisfied for the transgenic non-human mammals comprising α2/δ1 gene with a 290-like mutation. Thus the example provided does not commensurate with the scope and breadth of the instant claim.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (See In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their phenotypes or structure. Next, it is determined whether a representative number of species have been sufficiently described by relevant identifying characteristics.

Since the specification fails to disclose other claimed transgenic non-human mammals that contained sufficient number of examples of species of claimed genus of non-human mammals, it is not possible to envision the broadly claimed transgenic non-human mammals. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the transgenic non-human mammals as claimed has been defined only by a statement that α2/δ1 gene comprises 290-like mutation that conveyed no distinguishing information about the identity of the broadly claimed species. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of even a single member of this genus would not be representative of claimed genus of transgenic animal species and is insufficient to support the claim in its present scope.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims are drawn to a genetically modified, non-human mammals comprising α2/δ1 gene comprising 290-like mutation.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the prior art; (4) The level of one of ordinary skill; (5) The level of predictability in the art; (6) The amount of direction provided by the inventor; (7) The existence of working examples; and (8) The quantity of experimentation needed to make or use the invention based of the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). All of the wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below as to show that one of the ordinary skill in the art have to go through "undue experimentation" in order to practice the invention.

Nature of the invention: The invention relates to genetically modified, non-human mammals comprising α2/δ1 gene comprising 290-like mutation.

Breadth of the claims And Guidance of the Specification and The scope and breadth of the instant claims, read in the light of instant specification and the state of the art at the time of filing encompass transgenic non-human mammal comprising alpha2/delta1 gene with a 290-like mutation. Further the claim is read on numerous transgenic non-human mammals, such as mice, rats, rabbits, sheep, pigs, canine, feline, monkeys, kangaroos, echidnas, whales, other mammals etc., expressing a alpha2/delta1with said mutation. The claims encompass numerous transgenic non-human mammals having various unknown and unidentified phenotypes or having no phenotype.

With respect to instant claim the specification only discloses embodiment of the transgenic knock-in mouse that over expresses the whole alpha2/delta1 protein with R217A mutation. The application further defines a 290-like mutation in reference to α2/δ2 gene only but not with reference to alpha2/delta1 gene as claimed.

Specification does not enable any mutant non-human transgenic mammals that are expressing α2/δ1 gene with a 290-like mutation. The specification further fails to provide adequate guidance and evidence for how to make and use the claimed transgenic non-human mammals alpha2/delta1 gene with 290-like mutation. The specification also fails to disclose any phenotype of the claimed transgenic non-human

mammals. A transgenic non-human mammal having no phenotype is indistinguishable from a wild-type mammal and one skilled in the art at the time of the invention would not know how to use the claimed transgenic non-human mammals. Specification does not describe any mammalian species comprising α2/δ1 gene with a 290-like mutation and a significant phenotype that would enable to serve as a model for any art established human/animal diseases or human/animal conditions.

The specification thus fails to provide an enabling disclosure for the full scope and breadth of the invention as claimed. In the absence of adequate description of the enabled invention commensurate with the breadth and scope of the claim one of ordinary skill in the art would conclude that the claimed invention is unpredictable and would require an undue amount of experimentation to practice the full scope of the same. Applicants' attention is drawn to In re Shokal, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). The test is whether the species completed by applicants prior to the reference date or the date of the activity provided an adequate basis for inferring that the invention has generic applicability.

The level of one of ordinary skill in the Art at the Time of Invention: The level of one of ordinary skill in the art at the time of filing of the instant application is high requiring an advanced degree or training in the relevant field. The status of the art at the time of filing was such that said skilled in the art would not have been able to make or use the invention for its fully claimed scope without undue experimentation.

***State of the Art, the Predictability of the Art*:** At about the effective filing date of the present application art does not provide enablement for making a transgenic mammals that are expressing α2/δ1 gene with a 290-like mutation, as the art does not describe the existence of such a mutation or its consequences on the coded gene product or an animal expressing the same. Art is still unpredictable with regard to achieving a desired phenotype even in a mouse that is of substantial use or utility for example modeling human/non-human animal diseases or conditions.

Further the mere capability to perform gene transfer in a mouse is not enabling because a desired phenotype cannot be predictably achieved by simply introducing transgene constructs (Rulicke and Hubischer, Experimental Physiology 85: 589-601,

2000) of the types recited in the claims. Unpredictability of phenotypes in conventional transgene introduction, as is in the instant application, arises due to transgene random integration into the host genome and subsequent aberrations namely poor expression, temporally and/or spatially aberrant expression, position effects etc. Further unpredictability arises owing to the functional and physiological effects of the expressed transgene (foreign gene), interference of the redundant native genes, induction of compensatory processes, gene silencing effects as well as due to the influence of genetic background and the phenomenon of imprinting (reviewed in Rulicke and Hubischer, Experimental Physiology 85: 589-601, 2000; p.595 1st col. 1st ¶). Even if this were to be a knock in mutation in endogenous gene or a gene deletion or gene disruption there still exists unpredictability regarding the expression of a desired mutant phenotype exists because of the variations in the genetic background of strains or species of non-human mammal involved. Holschneider et al. Int J. Devl. Neuroscience 18:615-618, 2001, state that knocking out or insertion of a single gene may result in no phenotypic change. This may be the case, in particular, if there exist gene redundancy mechanisms whose presence may prevent abnormal phenotypes from becoming expressed. Conversely, single genes are often essential in a number of different behaviors and physiologic processes. Silence, ablation of an individual gene may prove so drastic as to be lethal, or so widespread as to create an amalgam of phenotypes whose interpretation becomes confounded by the interactions of the various new physiologic changes or behaviors." (See p. 615, col. 1-21). Holschneider et al., discuss various factors that contribute to the resulting phenotype of transgenic mice, including compensatory systems which may be activated to mask the resulting phenotype, these compensatory changes may be due to the differential expression of another gene, which may be regulated by the downstream product of, the ablated gene, as well as the variability in phenotypic characterization due to particular mouse strains (see p. 616, 1st column).

Amount of experimentation necessary: Because of the lack of working examples of a non-human mammal comprising α2/δ1 gene with 290-like mutation, insufficient guidance and direction provided by Applicant, the inherent unpredictability of the art, and the nature of the invention, one of skill in the art would be find it not enabling

to make and use a transgenic non-human mammal with said mutation without knowing what the claim encompasses further will not be able to predict a priori what the phenotypes of such non-human mammals and their use. Accordingly, in view of the lack of teachings or guidance provided by the specification with regard to an enabled description and use for a mammal comprising a comprising α2/δ1 gene with a 290-like mutation, absent guidance provided by the specification to overcome the art-recognized unpredictability regarding transgenic technology in non-human mammals, and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the claimed invention.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Dave Nguyen*, may be reached at **(571) 272-0731.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna
Patent Examiner
Art Unit 1633

SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER